

[0027] Examples of the disclosure relate to a method of inhibiting the growth of a tumor expressing a cancer or tumor antigen, by contacting the tumor with an effective amount of the isolated cells or compositions disclosed above. The contacting can be *in vitro* or *in vivo*. When the contacting is *in vitro*, the method can be used to test personalized therapy against a patient's tumor or to assay for combination therapies. When the contacting is *in vivo*, the method is useful to inhibit the growth of the tumor or cancer cell in a subject in need thereof, such as a human patient suffering from cancer and the patient receives an effective amount of the cells. In certain examples, the tumor is a solid tumor. An effective amount is administered alone or in combination with other therapies as described herein. In certain examples, the cancer/tumor targeted is a solid tumor or a cancer affecting the blood and/or bone marrow, e.g., multiple myeloma (MM). In certain examples the isolated cells are autologous to the subject being treated. In another example, the cells are allogeneic to the subject being treated. In another example, the method further comprises, or consists essentially of, or yet further consists of, administering to the subject an effective amount of a cytoreductive therapy. In a further example, the method further comprises the steps of isolating the cells to be administered to the subject, transducing the cells with an effective amount of an isolated nucleic acid encoding a CAR or BsAb-CAR as described herein, culturing the cells to obtain a population of CAR or BsAb-CAR encoding cells, that are optionally expanded and activated and then administering the cells to the patient.

[0027a] In another aspect, the present disclosure refers to an *in vitro* method of inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen, comprising contacting the cancer cell or tumor with the isolated cell as disclosed herein, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

[0027b] In another aspect, the present disclosure refers to use of an isolated cell as disclosed herein in the manufacture of a medicament for inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen in a subject, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

[0028] Also disclosed herein are kits comprising one or more of the above noted compositions and instructions for their use in the methods as disclosed herein.

[0028a] In another aspect, the present disclosure refers to a kit comprising a composition as disclosed herein and optionally, instructions for use.

[0029] The above compositions and methods are unique and overcome the limitation of the state of the art in that they provide a CAR cell that simultaneously secretes a NKG2D-based BsAb targeting a second tumor-associated antigen. The disclosed CAR NKG2D-based BsAb is exemplary only. This approach can be modified for any number of tumor antigens, as known in the art, e.g., EGFRVIII; CD70, mesothelin, CD123, CD19, CEA, CD133, Her2, see Townsend et al. (2018) J. Exp. & Clinical Cancer Res. 37:163.

[0030] The exemplary constructs were tested in a multiple myeloma model (MM). MM is a malignancy characterized by an accumulation of clonal plasma cells¹³. As noted above, current treatment regimens including chemotherapies, immunomodulatory drugs¹⁴, monoclonal antibodies¹⁵, and autologous or allogeneic transplantation often lead to remission, but nearly all patients eventually relapse and succumb to death due to return of

WHAT IS CLAIMED IS:

1. An isolated nucleic acid comprising:
a polynucleotide encoding a chimeric antigen receptor (CAR) comprising: (a) an antigen
5 binding domain that targets B-cell maturation antigen (BCMA); (b) a hinge domain; (c) a
transmembrane domain; (d) and an intracellular domain; and
a polynucleotide encoding a bispecific antibody comprising an antigen binding domain
that recognizes and binds NKG2D and an antigen binding domain that recognizes and binds
SLAMF7.
- 10 2. The isolated nucleic acid of claim 1, wherein the hinge domain comprises a CD8 α hinge
domain.
3. The isolated nucleic acid of claim 1 or 2, wherein the transmembrane domain comprises a
CD8 α transmembrane domain.
4. The isolated nucleic acid of any one of claims 1-3, wherein the intracellular domain
15 comprises a CD28 costimulatory signaling region or a 4-1BB costimulatory signaling region; and
a CD3 zeta signaling domain.
5. The isolated nucleic acid of any one of claims 1 to 4, wherein the antigen binding domain
that recognizes and binds NKG2D comprises three complementarity determining regions (CDRs)
an anti-NKG2D heavy chain encoded by:
20 CAAGTGCAGC TGGTTGAATC CGGTGGCGGT CTGGTCAAGC CGGGCGGCTC
TTTGCGTCTG AGCTGTGCCG CGTCGGGTTT TACCTTCAGC TCTTATGGTA
TGCATTGGGT GCGTCAGGCG CCTGGCAAAG GTCTGGAGTG GGTGCGTTC
ATCCGCTACG ATGGGTCTAA CAAATATTAT GCCGACTCAG TAAAAGGACG
CTTCACTATT AGCCGCGACA ATAGCAAAAA TACCCTGTAC CTGCAAATGA
25 ATAGCCTGCG CGCCGAAGAT ACCGCCGTTT ACTATTGCGC TAAAGATCGT
GGCCTGGGTG ATGGTACGTA CTTGATTAC TGGGGTCAGG GCACCACCGT
TACCGTTAGT TCA,
and three CDRs of anti-NKG2D light chain encoded by:

CAGTCAGCGC TTACGCAGCC GCGGTCGGTG TCGGGTTCCC CGGGTCAGTC
GATCACGATC AGCTGTAGTG GGAGCAGCTC CAACATCGGT AACAAACGCAG
TGAAGTGGTA TCAGCAACTG CCGGGAAAAG CGCCGAAACT GCTGATTTAC
TATGATGATT TGCTGCCAAG TGGAGTTAGT GACCGCTTTT CCGGCAGTAA
5 ATCGGGTACC TCGGCTTTTC TGGCTATTTT GGGTCTCCAG AGCGAGGATG
AAGCTGATTA TTATTGCGCC GCATGGGATG ATAGCTTAAA TGGCCCAGTT
TTTGGCGGCG GTACTAAACT GACCGTGCTG, or three CDRs of anti-NKG2D heavy chain
encoded by:

CAAGTGCAGCTGGTTGAATCCGGTGGCGGTCTGGTCAAGCCGGGCGGCTCTTTGCGT
10 CTGAGCTGTGCCGCGTCGGGTTTTACCTTCAGCTCTTATGGTATGCATTGGGTGCGTC
AGGCGCCTGGCAAAGGTCTGGAGTGGGTTCGTTTCATCCGCTACGATGGGTCTAACA
AATATTATGCCGACTCAGTAAAAGGACGCTTCACTATTAGCCGCGACAATAGCAAA
AATACCCTGTACCTGCAAATGAATAGCCTGCGCGCCGAAGATAACCGCCGTTTACTAT
TGCGCTAAAGATCGTGGCCTGGGTGATGGTACGTACTTCGATTACTGGGGTCAGGGC
15 ACCACCGTTACCGTTAGTTCAGGTGGGGGCGGCTCT and three CDRs of anti-NKG2D
light chain encoded by:

CAGCGCTTACGCAGCCGGCGTCGGTGTCGGGTTCCCCGGGTCAGTCGATCACGATCA
GCTGTAGTGGGAGCAGCTCCAACATCGGTAACAACGCAGTGAAGTGGTATCAGCAA
CTGCCGGGAAAAGCGCCGAAACTGCTGATTTACTATGATGATTTGCTGCCAAGTGGA
20 GTTAGTGACCGCTTTTCCGGCAGTAAATCGGGTACCTCGGCTTTTCTGGCTATTTTCGG
GTCTCCAGAGCGAGGATGAAGCTGATTATTATTGCGCCGCATGGGATGATAGCTTAA
ATGGCCCAGTTTTTGGCGGCGGTACTAAACTGACCGTGCTG.

6. The isolated nucleic acid of claim 5, wherein the antigen binding domain that recognizes
and binds NKG2D comprises:

25 a heavy chain variable region comprising the amino acid sequence encoded by:

CAAGTGCAGC TGGTTGAATC CGGTGGCGGT CTGGTCAAGC CGGGCGGCTC
TTTGCGTCTG AGCTGTGCCG CGTCGGGTTT TACCTTCAGC TCTTATGGTA
TGCATTGGGT GCGTCAGGCG CCTGGCAAAG GTCTGGAGTG GGTTGCGTTC

ATCCGCTACG ATGGGTCTAA CAAATATTAT GCCGACTCAG TAAAAGGACG
CTTCACTATT AGCCGCGACA ATAGCAAAAA TACCCTGTAC CTGCAAATGA
ATAGCCTGCG CGCCGAAGAT ACCGCCGTTT ACTATTGCGC TAAAGATCGT
GGCCTGGGTG ATGGTACGTA CTTGATTAC TGGGGTCAGG GCACCACCGT
5 TACCGTTAGT TCA,

and a light chain variable region comprising the amino acid sequence encoded by:

CAGTCAGCGC TTACGCAGCC GGCCTCGGTG TCGGGTCCC CGGGTCAGTC
GATCACGATC AGCTGTAGTG GGAGCAGCTC CAACATCGGT AACAACGCAG
TGAAGTGGTA TCAGCAACTG CCGGGAAAAG CGCCGAAACT GCTGATTTAC
10 TATGATGATT TGCTGCCAAG TGGAGTTAGT GACCGCTTTT CCGGCAGTAA
ATCGGGTACC TCGGCTTTTC TGGCTATTTC GGGTCTCCAG AGCGAGGATG
AAGCTGATTA TTATTGCGCC GCATGGGATG ATAGCTTAAA TGGCCCAGTT
TTTGGCGGCG GTACTAAACT GACCGTGCTG; or

a heavy chain variable region comprising the amino acid sequence encoded by:

15 CAAGTGCAGCTGGTTGAATCCGGTGGCGGTCTGGTCAAGCCGGGCGGCTCTT
TGCGTCTGAGCTGTGCCGCGTCGGGTTTTACCTTCAGCTCTTATGGTATGCATTGGGT
GCGTCAGGCGCCTGGCAAAGGTCTGGAGTGGGTTCGCTTCATCCGCTACGATGGGTC
TAACAAATATTATGCCGACTCAGTAAAAGGACGCTTCACTATTAGCCGCGACAATAG
CAAAAATACCCTGTACCTGCAAATGAATAGCCTGCGCGCCGAAGATACCGCCGTTT
20 ACTATTGCGCTAAAGATCGTGGCCTGGGTGATGGTACGTACTTCGATTACTGGGGTC
AGGGCACCAACCGTTACCGTTAGTTCAGGTGGGGGCGGCTCT, and a light chain variable
region comprising the amino acid sequence encoded by:

CAGCGCTTACGCAGCCGGCGTCGGGTGTCGGGTCCCCGGGTCAGTCGATCAC
GATCAGCTGTAGTGGGAGCAGCTCCAACATCGGTAACAACGCAGTGAAGTGGTATC
25 AGCAACTGCCGGGAAAAGCGCCGAAACTGCTGATTTACTATGATGATTTGCTGCCAA
GTGGAGTTAGTGACCGCTTTTCCGGCAGTAAATCGGGTACCTCGGCTTTTCTGGCTA
TTTCGGGTCTCCAGAGCGAGGATGAAGCTGATTATTATTGCGCCGCATGGGATGATA
GCTTAAATGGCCCAGTTTTTGGCGGCGGTACTAAACTGACCGTGCTG;or

an equivalent of each thereof, wherein an equivalent of a peptide has at least 90% amino acid identity to the peptide.

7. The isolated nucleic acid of any one of claims 1-6, wherein the antigen binding domain that recognizes and binds NKG2D comprises:

5 a heavy chain variable region comprising the amino acid sequence encoded by:

CAAGTGCAGC TGGTTGAATC CGGTGGCGGT CTGGTCAAGC CGGGCGGCTC
TTTGCGTCTG AGCTGTGCCG CGTCGGGTTT TACCTTCAGC TCTTATGGTA
TGCATTGGGT GCGTCAGGCG CCTGGCAAAG GTCTGGAGTG GGTTCGTTT
ATCCGCTACG ATGGGTCTAA CAAATATTAT GCCGACTCAG TAAAAGGACG
10 CTTCACCTATT AGCCGCGACA ATAGCAAAAA TACCCTGTAC CTGCAAATGA
ATAGCCTGCG CGCCGAAGAT ACCGCCGTTT ACTATTGCGC TAAAGATCGT
GGCCTGGGTG ATGGTACGTA CTTTCGATTAC TGGGGTCAGG GCACCACCGT
TACCGTTAGT TCA, and a light chain variable region comprising the amino acid sequence
encoded by:

15 CAGTCAGCGC TTACGCAGCC GGCGTCGGTG TCGGGTTCCC CGGGTCAGTC
GATCACGATC AGCTGTAGTG GGAGCAGCTC CAACATCGGT AACAACGCAG
TGAAGTGGTA TCAGCAACTG CCGGGAAAAG CGCCGAAACT GCTGATTTAC
TATGATGATT TGCTGCCAAG TGGAGTTAGT GACCGCTTTT CCGGCAGTAA
ATCGGGTACC TCGGCTTTTC TGGCTATTTT GGGTCTCCAG AGCGAGGATG
20 AAGCTGATTA TTATTGCGCC GCATGGGATG ATAGCTTAAA TGGCCCAGTT
TTTGGCGGCG GTACTAAACT GACCGTGCTG; or

a heavy chain variable region comprising the amino acid sequence encoded by:

CAAGTGCAGCTGGTTGAATCCGGTGGCGGTCTGGTCAAGCCGGGCGGCTCTT
TGCGTCTGAGCTGTGCCGCGTCGGGTTTTACCTTCAGCTCTTATGGTATGCATTGGGT
25 GCGTCAGGCGCCTGGCAAAGGTCTGGAGTGGGTTCGTTTCATCCGCTACGATGGGTC
TAACAAATATTATGCCGACTCAGTAAAAGGACGCTTCACTATTAGCCGCGACAATAG
CAAAAATACCCTGTACCTGCAAATGAATAGCCTGCGCGCCGAAGATACCGCCGTTT
ACTATTGCGCTAAAGATCGTGGCCTGGGTGATGGTACGTACTTCGATTACTGGGGTC
AGGGCACCAACCGTTACCGTTAGTTCAGGTGGGGGCGGCTCT, and a light chain variable
30 region comprising the amino acid sequence encoded by:

CAGCGCTTACGCAGCCGGCGTCGGTGTCTGGGTTCCCCGGGTCAGTCGATCAC
 GATCAGCTGTAGTGGGAGCAGCTCCAACATCGGTAACAACGCAGTGAAGTGGTATC
 AGCAACTGCCGGGAAAAGCGCCGAACTGCTGATTTACTATGATGATTTGCTGCCAA
 GTGGAGTTAGTGACCGCTTTTCCGGCAGTAAATCGGGTACCTCGGCTTTTCTGGCTA
 5 TTTCGGGTCTCCAGAGCGAGGATGAAGCTGATTATTATTGCGCCGCATGGGATGATA
 GCTTAAATGGCCCAGTTTTTGGCGGCGGTACTAACTGACCGTGCTG.

8. The isolated nucleic acid of any one of claims 1-7, wherein the antigen binding domain that recognizes and binds SLAMF7 comprises three CDRs encoded by:

10 AGCGTTACCG TGAGTACAGG CCAGGGCTGG TATGACATGG CACGTACAGC
 CATCATGACC TCGCGCGCAT GTTACTACGT CGCGTCAGAT GAATCGACGC
 CTCCTCGCT GCAAATGTAT GCAACCTCCA GCAGCAAAGA TGTTACCCTG
 ACCGCAAAGG ACAAGTTTAA ACAGAATTTG CGTACGGAGA GTGACTCCCC
 GCACATCATG GGAATCTGGG AGTTGGGTCA GGGGCCTCGT CAGAAGGTAT
 15 GGAACATGTG GTATACAACT TTTTCGTACG GCTCAGCAAA ATGCAGCTTG
 AAAGTGTCGG CAGGTCCGCG CGTGCTGGAG GCCGGTCCGC AGCAGCTGCA
 AGTCCAGTCT, and three CDRs encoded by:

AAACTTGAGT TGAAGACCGG TGCCGGCTTC ACCTTACCGA CCAGTTATCA
 TCAACAATGC TATTACGTGG CCCTGGACGA AGCACAGGTG AATTCAATTA
 20 CGTTTACGTT TGATACCGGC TCTGGCAGCG GTACATTTTCG TGATCCCGTG
 GGCACCTACC GCTATTCGGC GAGTTATATC TTGCTGAAAC CTTCCCAAGG
 TCCGAAACAG CAGTACTGGG CGGTTGGCAC CATTGTAGAC CAATCAGCCA
 AATGTACAAT CTCGGTTCGC GATGGTGTCA GTACGTCGAT GTCTAAGCAG
 TCACAGACAA TGGTTATCGA T or three CDRs encoded by:

25 CTCCGTGACGGTGTCTGACGGGCCAAGGATGGTACGATATGGCACGGACCGCGATTA
 TGACATCGCGGGCGTGCTATTACGTGGCCAGCGATGAGTCGACCCCTTCTCTCTGC
 AAATGTATGCCACCTCCTCTTCAAAGACGTGACTCTGACTGCGAAAGACAAATTTA
 AACAGAATCTGCGCACCGAAAGCGATAGCCCACATATCATGGGCATCTGGGAACTG
 GGCCAGGGCCCCCGCCAGAAAGTGTGGAACATGTGGTACACCACCTTCAGCTATGG

TTCGGCCAAATGTTCCCTGAAGGTATCAGCCGGCCCGCGCGTTCTTGAGGCGGGTCC
GCAGCAGCTGCAGGTACAGAGC, and three CDRs of encoded by:

AAACTGGAAGTCAAGACGGGTGCGGGATTTACCCTCCCTACGAGCTATCACCAGCA
GTGCTATTACGTGGCGCTTGACGAAGCGCAGGTGAACTCTATTACCTTTACCTTTGA

5 TACAGGATCAGGCAGCGGTACGTTCCGTGATCCGGTAGGTACGTACCGGTATAGTGC
AAGCTATATCCTTCTGAAACCTTCTCAGGGTCCGAAACAGCAGTACTGGGCGGTGGG
AACGATCGTGGACCAGTCTGCCAAATGTACAATTTAGTTTCGCGACGGAGTTAGCAC
CTCCATGAGCAAGCAGTCCCAAACCATGGTGATTGACTC.

10 9. The isolated nucleic acid of any one of claims 1-8, wherein the antigen binding domain
that recognizes and binds SLAMF7 comprises:

a heavy chain variable region comprising the amino acid sequence encoded by:

AGCGTTACCG TGAGTACAGG CCAGGGCTGG TATGACATGG CACGTACAGC
CATCATGACC TCGCGCGCAT GTTACTACGT CGCGTCAGAT GAATCGACGC

15 CTTCTCGCT GCAAATGTAT GCAACCTCCA GCAGCAAAGA TGTTACCCTG
ACCGCAAAGG ACAAGTTTAA ACAGAATTTG CGTACGGAGA GTGACTCCCC
GCACATCATG GGAATCTGGG AGTTGGGTCA GGGGCCTCGT CAGAAGGTAT
GGAACATGTG GTATACAACT TTTTCGTACG GCTCAGCAA ATGCAGCTTG
AAAGTGTCCG CAGGTCCGCG CGTGCTGGAG GCCGGTCCGC AGCAGCTGCA

20 AGTCCAGTCT, and a light chain variable region comprising the amino acid sequence encoded
by:

AAACTTGAGT TGAAGACCGG TGCCGGCTTC ACCTTACCGA CCAGTTATCA
TCAACAATGC TATTACGTGG CCCTGGACGA AGCACAGGTG AATTCAATTA
CGTTTACGTT TGATACCGGC TCTGGCAGCG GTACATTTTCG TGATCCCGTG

25 GGCACCTACC GCTATTCGGC GAGTTATATC TTGCTGAAAC CTTCCCAAGG
TCCGAAACAG CAGTACTGGG CGGTTGGCAC CATTGTAGAC CAATCAGCCA
AATGTACAAT CTCGGTTCGC GATGGTGTCA GTACGTCGAT GTCTAAGCAG
TCACAGACAA TGGTTATCGA T; or

a heavy chain variable region comprising the amino acid sequence encoded by:

CTCCGTGACGGTGTGCGACGGGCCAAGGATGGTACGATATGGCACGGACCGCG
ATTATGACATCGCGGGCGTGCTATTACGTGGCCAGCGATGAGTCGACCCCTTCCTCT
CTGCAAATGTATGCCACCTCCTCTTCAAAAGACGTGACTCTGACTGCGAAAGACAAA
TTTAAACAGAATCTGCGCACCGAAAGCGATAGCCCACATATCATGGGCATCTGGGA
5 ACTGGGCCAGGGCCCCCGCCAGAAAGTGTGGAACATGTGGTACACCACCTTCAGCT
ATGGTTCGGCCAAATGTTCCCTGAAGGTATCAGCCGGCCCGCGCGTTCTTGAGGCGG
GTCCGCAGCAGCTGCAGGTACAGAGC, and a light chain variable region comprising the
amino acid sequence encoded by:

AAACTGGA ACTCAAGACGGGTGCGGGATTTACCCTCCCTACGAGCTATCACC
10 AGCAGTGCTATTACGTGGCGCTTGACGAAGCGCAGGTGAACTCTATTACCTTTACCT
TTGATACAGGATCAGGCAGCGGTACGTTCCGTGATCCGGTAGGTACGTACCGGTATA
GTGCAAGCTATATCCTTCTGAAACCTTCTCAGGGTCCGAAACAGCAGTACTGGGCGG
TGGGAACGATCGTGGACCAGTCTGCCAAATGTACAATTTTCAGTTCGCGACGGAGTTA
GCACCTCCATGAGCAAGCAGTCCCAAACCATGGTGATTGACTCT; or

15 an equivalent of each thereof, wherein an equivalent of a peptide has at least 90% amino
acid identity to the peptide.

10. The isolated nucleic acid of any one of claims 1-9, wherein the antigen binding domain
that recognizes and binds SLAMF7 comprises:

20 a heavy chain variable region comprising the amino acid sequence encoded by:
AGCGTTACCG TGAGTACAGG CCAGGGCTGG TATGACATGG CACGTACAGC
CATCATGACC TCGCGCGCAT GTTACTACGT CGCGTCAGAT GAATCGACGC
CTTCCTCGCT GCAAATGTAT GCAACCTCCA GCAGCAAAGA TGTTACCCTG
ACCGCAAAGG ACAAGTTTAA ACAGAATTTG CGTACGGAGA GTGACTCCCC
25 GCACATCATG GGAATCTGGG AGTTGGGTCA GGGGCCTCGT CAGAAGGTAT
GGAACATGTG GTATACTACT TTTTCGTACG GCTCAGCAA ATGCAGCTTG
AAAGTGTCGG CAGGTCCGCG CGTGCTGGAG GCCGGTCCGC AGCAGCTGCA
AGTCCAGTCT and a light chain variable region comprising the amino acid sequence encoded
by:

AAACTTGAGT TGAAGACCGG TGCCGGCTTC ACCTTACCGA CCAGTTATCA
TCAACAATGC TATTACGTGG CCCTGGACGA AGCACAGGTG AATTCAATTA
CGTTTACGTT TGATACCGGC TCTGGCAGCG GTACATTTTCG TGATCCCGTG
GGCACTTACC GCTATTCGGC GAGTTATATC TTGCTGAAAC CTTCCCAAGG
5 TCCGAAACAG CAGTACTGGG CGGTTGGCAC CATTGTAGAC CAATCAGCCA
AATGTACAAT CTCGGTTCGC GATGGTGTCA GTACGTCGAT GTCTAAGCAG
TCACAGACAA TGGTTATCGA T; or

a heavy chain variable region comprising the amino acid sequence encoded by:

CTCCGTGACGGTGTGACGGGCCAAGGATGGTACGATATGGCACGGACCGCG
10 ATTATGACATCGCGGGCGTGCTATTACGTGGCCAGCGATGAGTCGACCCCTTCCTCT
CTGCAAATGTATGCCACCTCCTCTTCAAAAGACGTGACTCTGACTGCGAAAGACAAA
TTTAAACAGAATCTGCGCACCGAAAGCGATAGCCCACATATCATGGGCATCTGGGA
ACTGGGCCAGGGCCCCCGCCAGAAAGTGTGGAACATGTGGTACACCACCTTCAGCT
ATGGTTCGGCCAAATGTTCCCTGAAGGTATCAGCCGGCCCGCGCGTTCTTGAGGCGG
15 GTCCGCAGCAGCTGCAGGTACAGAGC, and a light chain variable region comprising the
amino acid sequence encoded by:

AAACTGGA ACTCAAGACGGGTGCGGGATTTACCCTCCCTACGAGCTATCACC
AGCAGTGCTATTACGTGGCGCTTGACGAAGCGCAGGTGAACTCTATTACCTTTACCT
TTGATACAGGATCAGGCAGCGGTACGTTCCGTGATCCGGTAGGTACGTACCGGTATA
20 GTGCAAGCTATATCCTTCTGAAACCTTCTCAGGGTCCGAAACAGCAGTACTGGGCGG
TGGAACGATCGTGGACCAGTCTGCCAAATGTACAATTTAGTTCGCGACGGAGTTA
GCACCTCCATGAGCAAGCAGTCCCAAACCATGGTGATTGACTCT.

11. The isolated nucleic acid of any one of claims 1-10, wherein the antigen binding domain
25 that recognizes and binds NKG2D is a single chain variable fragment (scFV) and the antigen
binding domain that recognizes and binds SLAMF7 is a single chain variable fragment (scFv).

12. The isolated nucleic acid of any one of claims 1-11, wherein the antigen binding domain
that targets BCMA comprises three CDRs encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCACCAG
 ATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGAAGAT
 CAGCTGCAAGGCCTCCGGCTACACCTTCCGGCACTACAGCATGAACTGGGTGAAAC
 AGGCCCTGGCAAGGGCCTGAAGTGGATGGGCGGATCAACACCGAGAGCGGCGTG
 5 CCCATCTACGCCGACGACTTCAAGGGCAGATTCGCCTTCAGCGTGGAACCAGCGC
 CAGCACCGCCTACCTGGTGATCAACAACCTGAAGGACGAGGATACCGCCAGCTACT
 TCTGCAGCAACGACTACCTGTACAGCCTGGACTTCTGGGGCCAGGGCACCGCCCTGA
 CCGTGTCCAGC, and three CDRs encoded by:
 GACATCGTGCTGACCCAGAGCCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGAGAGC
 10 CACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTGATCT
 ACTGGTATCAGCAGAAGCCTGGCCAGCCCCCCCCACCCTGCTGATCCAGCTGGCTAGCA
 ATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGACTTC
 ACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCTGCA
 GAGCCGGACCATCCCCCGGACCTTTGGCGGAGGAACAAAGCTGGAAATCAAG, three
 15 CDRs encoded by:
 ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCACCAG
 ATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGAAGAT
 CAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTGAAAA
 GAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAAGAGA
 20 GCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAACCAGCGC
 CAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCACCTACT
 TTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCCAGCGTG
 ACCGTGTCCAGC, and three CDRs encoded by:
 GACATCGTGCTGACCCAGAGCCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGAGAGC
 25 CACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTGATCC
 ACTGGTATCAGCAGAAGCCCGGCCAGCCCCCCCCACCCTGCTGATCCAGCTCGCCAGC
 AATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGACTT
 CACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCTGC
 AGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAAGCTGGAAATCAAG, or
 30 three CDRs encoded by:

CAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGAA
GATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTGA
AAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAAG
AGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTTCGCCTTCAGCCTGGAAACCA
5 GCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCACC
TACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCAGC
GTGACCGTGTCCAGC, and three CDRs encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGAGAGC
CACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTGATCC
10 ACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCCAGC
AATGTGCAGACCGGCGTGCCCGCCAGATTACAGCGGCAGCGGCAGCAGAACCGACTT
CACCTTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCTGC
AGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG,

13. The isolated nucleic acid of any one of claims 1-12, wherein the antigen binding domain that targets BCMA comprises:

a heavy chain variable region comprising the amino acid sequence encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
20 AGATCAGCTGCAAGGCCTCCGGCTACACCTTCCGGCACTACAGCATGAACTGGGTG
AAACAGGCCCCTGGCAAGGGCCTGAAGTGGATGGGCCGGATCAACACCGAGAGCG
GCGTGCCCATCTACGCCGACGACTTCAAGGGCAGATTTCGCCTTCAGCGTGGAACC
AGCGCCAGCACCGCCTACCTGGTGATCAACAACCTGAAGGACGAGGATACCGCCAG
CTACTTCTGCAGCAACGACTACCTGTACAGCCTGGACTTCTGGGGCCAGGGCACCGC
25 CCTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid
sequence encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCTACTGGTATCAGCAGAAGCCTGGCCAGCCCCCACCCTGCTGATCCAGCTGGCT
30 AGCAATGTGCAGACCGGCGTGCCCGCCAGATTACAGCGGCAGCGGCAGCAGAACCGA

CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGAACAAAGCTGGAAATCAAG;

or

a heavy chain variable region comprising the amino acid sequence encoded by:

5 ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
AGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTG
AAAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAA
GAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAAACC
10 AGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCAC
CTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCAG
CGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid

sequence encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
15 GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG;

20 or

a heavy chain variable region comprising the amino acid sequence encoded by:

CAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACA
GTGAAGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTG
GGTGAAAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGA
25 CAAGAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAA
ACCAGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGC
CACCTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCAC
CAGCGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid
sequence encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCCGGCCAGCCCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
5 CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAAGTGGAAATCAAG;

or

an equivalent of each thereof, wherein an equivalent of a peptide has at least 90% amino acid identity to the peptide.

10

14. The isolated nucleic acid of any one of claims 1-13, wherein the antigen binding domain that targets BCMA comprises:

a heavy chain variable region comprising the amino acid sequence encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
15 CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
AGATCAGCTGCAAGGCCTCCGGCTACACCTTCCGGCACTACAGCATGAACTGGGTG
AAACAGGCCCCTGGCAAGGGCCTGAAGTGGATGGGCCGGATCAACACCGAGAGCG
GCGTGCCCATCTACGCCGACGACTTCAAGGGCAGATTCGCCTTCAGCGTGGAACC
AGCGCCAGCACCGCCTACCTGGTGATCAACAACCTGAAGGACGAGGATACCGCCAG
20 CTACTTCTGCAGCAACGACTACCTGTACAGCCTGGACTTCTGGGGCCAGGGCACCGC
CCTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid
sequence encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
25 ATCTACTGGTATCAGCAGAAGCCTGGCCAGCCCCCCCACCCTGCTGATCCAGCTGGCT
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGAACAAAGCTGGAAATCAAG;

or

30 a heavy chain variable region comprising the amino acid sequence encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
AGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTG
AAAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAA
5 GAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAAACC
AGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCAC
CTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCAG
CGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid
sequence encoded by:

10 GACATCGTGCTGACCCAGAGCCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCGGCCAGCCCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
15 GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG;
or

a heavy chain variable region comprising the amino acid sequence encoded by:

CAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACA
GTGAAGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTG
20 GGTGAAAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGA
CAAGAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAA
ACCAGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGC
CACCTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCAC
CAGCGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid
25 sequence encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCGGCCAGCCCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA

CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG.

15. The isolated nucleic acid of any one of claims 1-14, wherein the hinge domain comprises
5 CTCGAGCCCCAAATCTTGTGACAAAACCTCACACATGCCCACCGTGCCCG, the
transmembrane domain comprises
TTTTGGGTGCTGGTGGTGGTTGGTGGAGTCCTGGCTTGCTATAGCTTGCTAGTAACA
GTGGCCTTTATTATTTTCTGGGTG, the CD3 zeta signaling domain comprises
AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACCAGCAGGGCCAGAACC
10 AGCTCTATAACGAGCTCAATCTAGGACGAAGAGAGGAGTACGATGTTTTGGACAAG
AGACGTGGCCGGGACCCTGAGATGGGGGGAAAGCCGAGAAGGAAGAACCCTCAGG
AAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGGAGGCCTACAGTGAGATT
GGGATGAAAGGCGAGCGCCGGAGGGGCAAGGGGCACGATGGCCTTTACCAGGGTCT
CAGTACAGCCACCAAGGACACCTACGACGCCCTTCACATGCAGGCCCTGCCCCCTCG
15 CTAA, or an equivalent of each thereof, and optionally the intracellular domain comprises a
CD28 costimulatory signaling region comprising
AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAACATGACTCCCCGCCG
CCCCGGGCCCCACCCGCAAGCATTACCAGCCCTATGCCCCACCACGCGACTTCGCAGC
CTATCGCTCC or an equivalent thereof, or a 4-1BB costimulatory signaling region comprising
20 AAACGGGGCAGAAAGAAACTCCTGTATATATTCAAACAACCATTTATGAGACCAGT
ACAAACTACTCAAGAGGAAGATGGCTGTAGCTGCCGATTTCCAGAAGAAGAAGAAG
GAGGATGTGAACTG, or an equivalent thereof, wherein an equivalent of a peptide has at least
90% amino acid identity to the peptide.

16. A vector comprising the isolated nucleic acid of any one of claims 1-15.

25

17. The vector of claim 16, wherein the vector is a plasmid, and optionally further comprises
a promoter to regulate expression of the polynucleotide.

18. The vector of claim 16, wherein the vector is a viral vector, optionally selected from the group of a retroviral vector, a lentiviral vector, an adenoviral vector, and an adeno-associated viral vector, and further optionally a promoter to regulate expression of the polynucleotide.
19. An isolated cell comprising the isolated nucleic acid of any one of claims 1-15 or the
5 vector of any one of claims 16-18.
20. The isolated cell of claim 19, wherein the cell is a prokaryotic cell or a eukaryotic cell.
21. The isolated cell of claim 19 or 20, wherein the cell is an immune cell, optionally a T-cell, a B cell, a NK cell, a dendritic cell, a myeloid cell, a monocyte, or a macrophage.
22. The isolated cell of claim 19 or 20, wherein the cell is a stem cell, optionally an induced
10 pluripotent stem cell (iPSC).
23. A composition comprising the isolated nucleic acid of any one of claims 1-15 or the vector of any one of claims 16-18 or the isolated cell of any one of claims 19-22, and optionally, a pharmaceutically acceptable carrier.
24. An isolated complex comprising an isolated cell comprising of any one of claims 19-22
15 bound to a cell expressing NKG2D.
25. An isolated complex comprising the isolated cell of any one of claims 19-22 bound to a cancer or tumor antigen or a fragment thereof, wherein the cancer or tumor antigen is BCMA or SLAMF7.
26. A method of producing a CAR expressing cell comprising transducing an isolated cell
20 with the vector of any one of claims 16-18.
27. The method of claim 26, wherein the isolated cell is T-cells, B cells, NK cells, dendritic cells, myeloid cells, monocytes, or macrophages.
28. An *in vitro* method of inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen, comprising contacting the cancer cell or tumor with the isolated cell of claim
25 19 or claim 20, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

29. Use of an isolated cell of claim 19 or claim 20 in the manufacture of a medicament for inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen in a subject, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

5 30. The use of claim 29, wherein the isolated cells are autologous or allogeneic to the subject being treated.

31. The use of claim 29, wherein the isolated cells are allogenic to the subject being treated.

32. A kit comprising a composition of claim 23 and optionally, instructions for use.